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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,006	11/17/2003	Daniel Dupret	58763.000026	5724
21967	7590	05/16/2006	EXAMINER	
HUNTON & WILLIAMS LLP INTELLECTUAL PROPERTY DEPARTMENT 1900 K STREET, N.W. SUITE 1200 WASHINGTON, DC 20006-1109			GUIDRY, GUY L	
		ART UNIT	PAPER NUMBER	
		1636		

DATE MAILED: 05/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/713,006	DUPRET ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Guy Guidry, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 03 March 2006.  
 2a) This action is FINAL.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1,3,6-14, 16-19 and 21-23 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1,3,6-14, 16-19 and 21-23 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on 11/17/2003 is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
     1. Certified copies of the priority documents have been received.  
     2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
     3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|  | 6) <input type="checkbox"/> Other: _____                                    |

**DETAILED ACTION**

Response filed 3 March 2006 to the Office Action mailed 3 November 2005 is acknowledged. Claims 1, 3, 6-14, 16-19 and 21-23 are pending in this application. Claims 1, 3, 6, 8-14, 16, 17 and 21-23 have amended. Claims 2, 4, 5, 15, 20 and 24-27 have been canceled. Claims 1, 3, 6-14, 16-19 and 21-23 are under consideration in this Action. All objections/rejections not repeated herein are hereby withdrawn. Previous rejections to claims 2, 4, 5, 15, 20 and 24-27 have been rendered moot by Applicant's cancellation of those claims. Where applicable, a response to Applicant's arguments and amendments will be set forth immediately following any objections/rejections repeated herein.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claims 1, 3, 6-14, 16-19 and 21-23 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

Applicants argue that claim 1, as amended, does not contain the language in previous claim I to which the Examiner pointed in making the rejection based on indefiniteness, i.e., "heteroduplex polynucleotide comprises at least one annealed fragment," "homologous heteroduplex," "one homologous heteroduplex," "until "

"said" before "fragment", "preparing" in the preamble and "exposing at least one homologous heteroduplex." Applicant argues that one of skill in the art would clearly understand the metes and bounds of claim 1, as amended and that the claim clearly and precisely delineates the scope of Applicants' inventive subject matter to the skilled artisan.

*Response to Applicant's amendments and arguments*

While claim 1 has been amended to modify phrasing that was particularly pointed out in the previous Action as contributing to indefiniteness, the amendments one do not fully correct the ambiguity and vagueness that arise from interpretation of this claim. Amended claim 1 (and dependent claims) remains vague and indefinite and as written is directed to action steps and elements which do not interrelate. The claim is drawn to a method of obtaining polynucleotide fragments comprising:

(a) obtaining a library of homologous polynucleotides from a parental polynucleotide by mutagenesis.

Homologous polynucleotides, defined in the disclosure, "differ from each other at least at one corresponding residue position. Thus, as used herein, homologous encompasses what is sometimes referred to as partially heterologous" (¶18 of the specification) Further, parental polynucleotide and parent are defined as interchangeable synonyms that refer to the polynucleotides that are fragmented to create donor fragments. In the present invention, the *parental polynucleotides* are generally *homologous heteroduplex polynucleotides* (¶21). (emphasis added).

Further, polynucleotide library and DNA library refer to a group, pool or bank of polynucleotides containing at least two homologous polynucleotides, particularly homologous heteroduplex polynucleotides (¶0023).

The homologous polynucleotides of 1(a) are parental polynucleotides which may also be *homologous heteroduplex polynucleotide fragments* even before the denaturing and hybridizing step of 1(b). In other words, the beginning substrate, i.e., the homologous polynucleotides, is a heteroduplex polynucleotide. Due to ambiguities with respect of definitions of phrases provided in the disclosure and recited in the claim, precisely what is being claimed by Applicant is not explicitly clear.

In sum, the invention of claim 1 is not clearly defined, because as written, the claim comprises limitations that are redundant, vague and indefinite and lacking clear metes and bounds. Therefore, rejection of claim 1, and claims which depend from claim 1 dependent claims, under the second paragraph of 35 U.S.C. 112 stands.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

*Response to Applicant's amendments and arguments*

This rejection of the instant claims under 35 U.S.C. 102(e) as being anticipated by Arnold et al. (US 6,537,746) is of record.

Applicants argue persuasively that the instant invention, which involves cleaving heteroduplex polynucleotides and denaturing the cleaved polynucleotides is not anticipated by the Arnold '746 patent, which does not disclose obtaining polynucleotide fragments by denaturing cleaved heteroduplex polynucleotides. Further, the Office agrees that that the Arnold '746 patent does not disclose that a heteroduplex polynucleotide is cleaved by proteins of a polynucleotide repair system which can cleave mismatched base pairs and that a cleaved heteroduplex is denatured to obtain fragments. Therefore, rejection of the instant claims under 35 U.S.C. 102(e) as being anticipated by Arnold et al. (US 6,537,746) is hereby withdrawn.

**Claims 1, 3, 6, 7, 9, 12, 16, 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Tsai-Wu et al. (Analytical Biochemistry, 1999, 275: 127-129).**

The claims have been given broadest possible interpretation. Tsai-Wu et al. teach M13mm3 and M13mm4 phage, which contain a one base pair mismatch, was used as template for PCR (meeting the limitation claim 1(a) mutagenesis (by PCR per ¶48 of the instant specification, and Taq polymerase is employed, a polymerase known to a person of skill in the art to introduce errors, meeting the limitation of claims 6 and 16). The DNAs were denatured with 0.1 N NaOH to release the unbiotinylated single-

stranded PCR product. The unbound A strand and the unbound complementary G strand were recovered from the respective tubes, mixed in a new tube, and renatured (p. 128, col. 1, ¶2) (meeting the limitation of denaturing and hybridizing to form heteroduplex polynucleotides of claim 1(b) and claim 9).

Two restriction sites were designed at the mismatch site so that the T/A homoduplex and the G/A homoduplex can be cleaved by the restriction enzymes JV<sub>s</sub>J~ and JV<sub>hel</sub> or the Escherichia coli mutY gene product, which possesses both glycosylase (claim 12) and apurinic/apyrimidinic lyase activity, can recognize a G/A mismatch in the DNA duplex, remove the adenine base, and subsequently produce a cleavage at the phosphodiester bond immediately downstream of the A base (p. 128, col. 1, ¶2 to col. 2) (meeting the limitation of 1(c) cleaving the heteroduplex by using a protein of a polynucleotide repair system)

The cleavage products were then fractionated on a denaturing gel (p.129, Fig. 2B) (meeting the limitation of step 1(D) and claim 7, because the fragments are non-identical). The entire method is performed in vitro (claim3). With respect to claim 21, the phrases partial digestion and partial cleavage are not particularly limiting. The instant disclosure provides scant guidance with respect to partial digestion, providing simply that "In still another embodiment, partial digestion of mismatches is achieved so that all mismatches are not cleaved" (¶56). It is considered, absent evidence to the contrary, that at least some minute portion of the heteroduplex of Tsai-Wu would be partially digested in view of the definition given in the instant disclosure.

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Therefore, claims 1, 3, 6, 7, 9, 12, 16, 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Tsai-Wu et al.

***Conclusion***

No claims are allowed.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Guy Guidry, Ph.D. whose telephone number is 571-272-7928. The examiner can normally be reached on Monday through Friday 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) (<http://pair-direct.uspto.gov>) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Guy Guidry, Ph.D.

Examiner

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DANIEL M. SULLIVAN  
PATENT EXAMINER